Universidade do Minho
Escola de Economia e Gestão

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Pharmaceutical Reference Pricing Schemes and Their Policy Implications

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Dissertação de Mestrado
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"Pharmaceutical Reference Pricing Schemes and Their Policy Implications".

Abstract

The increasing costs of health services stressed the need to control and contain expenditure. The Pharmaceutical sector has been chosen by many governments as a generous field for such containment. That way, the present thesis analyses one of the most popular regulatory policies in force, the reference pricing schemes.

Through the thesis, we provide a review of published literature on the theme, underlining effects and consequences of the policy discussed in the economic literature. We then develop a theoretical model to derive the implications of the policy introduction. We conclude that the model built is able to capture main effects predicted by the economic literature. The policy introduction produces a sharp reduction of prices of all firms in the cluster and reduction in third payer expenditure. However, effects on consumer surplus are ambiguous. Final discussion on present thesis relates to the scheme engineering in order to power the effect of the policy. Using the model built we present strategies that policy maker might use to increase welfare.

“Esquemas de Preços de Referência Farmacêuticos e suas Implicações de Política”.

Resumo.

Os custos crescentes dos serviços de saúde salientaram a necessidade de controlar e conter a despesa em saúde. O sector farmacêutico foi escolhido por vários governos como um campo generoso para tal contenção. Dessa forma, a presente tese analisa uma das políticas de regulação mais populares em vigor, os esquemas de preços de referência.

Ao longo da tese, realizamos uma revisão da literatura publicada sobre o tema, sublinhando efeitos e consequências da política discutidos na literatura económica. Em seguida, desenvolvemos um modelo teórico que nos permite derivar implicações da introdução da politica. Concluímos que o modelo construído é capaz de capturar os principais efeitos previstos pela literatura económica. A introdução da medida produz uma redução significativa dos preços de todas as empresas no grupo farmacêutico e uma redução das despesas do financiador. Contudo, os efeitos sobre o excedente do consumidor são ambíguos. A discussão final desta tese relaciona-se com a engenharia do esquema de forma a potenciar os seus efeitos. Usando o modelo, apresentamos estratégias que o decisor de política pode usar para aumentar o bem-estar social.

Content

Acronyms List

ATC – Anatomical Therapeutic Chemical Code

BI – Brand Independence

GPR – Generic Reference Pricing

OECD – Organization for Economic Co-operation and Development

r – Reference price

R&D – research and development

RP – Reference Pricing

RPS- Reference Pricing System

TPR – Therapeutic Reference Pricing

USA – United States of America

WHO – World Health Organization

1. Introduction

During the last few decades we have been observing a clear development of the medical science. This development, however, has been costly for the most developed western countries, running increasing health expenses. Higher and increasing complexity in technologies, rising specialization of medical professionals, growing demand for health services and growing scale of the institutions contributed to the increase in health expenses. In countries with a clear state intervention this warning bells became amplified by the need to control the growth of public healthcare expenditure. With such pressure on decision makers, several policies have been tried during this time period. Although health care systems and services are some of the most complex institutions, with massive inefficiencies, one of the main focuses for this containment has been the pharmaceutical industry, often seen by the public opinion as a high profits sector.

The increasing costs of health services left the majority of the world's population without access to the most expensive health treatments. However, the social importance given to the value of life and the randomness of the disease epidemiology, created the consciousness that no one should be left without treatment, just because its price is not affordable at a given time. This market failure raised the need for insurance, whether it comes from a public or a private entity. The increase in insurance plans and systems left the demand for health quite insensitive to prices, which drove away competition in this market. It is in this conjuncture that RPS emerges as a policy able to, despite saving the access to health from most of the demand, transfer some of the expenditure to the consumer and breaking its insensibility to the price (Miraldo, 2009). Although competition is something desirable, within the pharmaceutical market under patent drugs are wittingly protected given the investments in R&D made to create the new drug. That is the reason why in the majority of the countries RPS is only implemented after the expiry of the branded drug patent[1].

During the last decade Portugal adopted a reference pricing system (RPS) that defined the most expensive generic as the reference (r) for the scheme. Although there have been some changes during the last few years, the scheme now defines the mean of the five cheapest generics, within the market, as reference. Looking at international experience we find even bigger heterogeneity in the design of the policies adopted. So much discrepancy invites us to, imbued in

[1] R&D issues will be discussed in the R&D and market entry topic.

the spirit of the Alvin Roth "Economist as Engineer", look for the best design for the market, or, at least, for indications on the policy implications. Of course our intentions with the present thesis are substantially more modest than to design a market structure as Alvin Roth has been doing during the last few decades. However, keeping in mind that this is an academic work we intend to draw some perspectives on the implications of the policy introduction, and how the manipulations of the variables of the policy enhances those implications.

The present thesis is structured as follows, in the first section we look at the literature on the theme presenting it in different perspectives. This way, we look at institutional background, trying to understand the design of the policy and how and when the policy was implemented in different countries. We then proceed to a description of the several versions of the policy, particularly on the differences between endogenous and exogenous reference pricing and therapeutic and generic reference pricing. The analysis focuses on the implications derived of each version and explored in the economic published literature. The implications of the policy on research and development and market entry are then addressed with some special focus on the determinants of generic entry, and the conditions for a sustainable research and development investments.

In the second section of the thesis we approach the question under study with a theoretical model. We apply a Hotelling model with two horizontally differentiated generic firms and a vertically differentiated brand firm. Such construction allows us to make a static analysis of the market deriving the policy effect on prices, demands, profits. Finally we look at welfare effects of a shift in the weight of the cheapest generic on the market in the reference scheme. In this last part of the thesis we analyze utility derived from consumption, firm profits, third-payer expenditures and social welfare. As we will discuss, the model allows us to derive some intriguing conclusions on the value of brand-generic differentiation and on the meaning of such differentiation.

2 Institutional Background and Literature Review

2.1 Reference Pricing

From either the demand or supply side policies tried in the sector, this thesis underlines the RPS. The regulatory policy strategy under focus relies substantially on generic market entry, after the term of the patent protection. This way, a functional RPS implies the creation of a cluster after the generic entry. The referred cluster is the set of drugs able to reproduce identical therapeutic effects, or with the same chemical composition. Depending on the methodology chosen to cluster drugs, it may be called therapeutic or generic RP. We will take a closer look on these two kinds of RP ahead. Once there is more than one drug within a cluster, the reference might be set depending on market variables. Despite the several possible formulations of a RP system it can be generalized as a function of consumer's expenditure when buying a drug of price equal to P:

$$\mathrm{C} = \begin{cases} \alpha P & if\ P < r \\ (P - \mathrm{r}) + \alpha P & if\ P > r \end{cases}, \qquad (1)$$

where r is the reference price and $\alpha \in (0,1)$ is the coinsurance rate and C is the consumer's expenditure. In this simple scheme, it is clear that if a consumer buys a drug priced below the reference price r, then, faces a price equal to the amount of copayment set by the authorities times the price charged by the company. However, if the same consumer buys the expensive drug, above the reference price, pays the difference between prices, plus the copayment percentage times the price charged. Some systems may set the copayment to zero (α = 0), leaving no expense to the consumer in the case of choosing the drug priced below r.

Generally reference pricing is not a pricing strategy, in fact, it is a reimbursement strategy where drug prices are affected in an indirect fashion (Miraldo, 2009, Dylst et al, 2012). Indeed, in several countries governments have tried other solutions that do not depend on the behavior of the agents in the market, like price reductions by decree (Danzon and Ketcham, 2004), or price cap regulations (Brekke et al, 2011). Unlike a pure reimbursement system, where part of the price is supported by the insurer, regardless of the price charged, in a reference pricing the insurer supports a lump sum indexed to a reference previously set. As we will state ahead, the reference value can either be endogenously found in the market, or discretionally defined by the policy maker, and thus exogenously set. Therefore, despite of the

consumer's choice, the third party preserves its expense, leaving the payment of the difference between the reference price and the price of the drug of his choice to the purchaser.

As described, in this system, the different competitors in the market are not limited in their pricing (Ghislandi, 2009). The possibility of setting prices freely raises the questions of how should firms behave before the rules are set in the market. Nevertheless, the copayment exposure limits severely their options, as price sensitive consumers will be deviated to the competitors, thus forcing producers to reduce their prices (Mestre-Ferrandiz, 2003). This mechanism of increasing competition for the consumers' demand drives us to the core of the RPS. Puig-Junoy (2010) in a literature review on the theme, using 16 papers for several european pharmaceutical markets, concluded that RPS managed to reduce generic prices. Nonetheless, such reduction is more evident in branded drugs than generics. Simultaneously, generic drugs under the reference tend not to reduce its price until reference price is reduced, even when there are cheaper drugs in the market. Neeraj et al. (2009) reached some different conclusions. Using data from 19 countries from 1992 to 2004, the authors try to isolate the influence of each regulatory policy in the pharmaceutical market revenues. Surprisingly, the authors conclude that RPS is the policy with less effect on revenues. Either direct price control or economic evaluation seem to have more impact on revenues, even so, the authors recognize that in the absence of price control the effect of RPS increases to 10,5% of revenues reduction.

Although, according to most literature, the policy effects worldwide have been interesting, some note should be taken on other policy strategies that can muscle RPS and avoid opportunistic behaviors as those described above. Gonzalez et al. (2006) underlined the role of physicians in the introduction of new cheaper generics. The authors used the UK market of fluoxetine[2] to conclude that after generic entry, and the decrease in marketing expenditure from the brand firm, prescriptions shifted to other molecules under patent protection. Such prescribing behavior not only decreased brand share, but the entire molecule market share, keeping expenditure. This shift shows how pharmaceutical firms are able to avoid price competition through advertising and other market strategies. The influence of persuasive advertising and marketing strategies on physicians is discussed by Konigbauer (2007) in a theoretical model of vertical differentiation with two periods. The author concludes that unlike economic literature suggests, persuasive advertising, in pharmaceutical markets, may not reduce welfare, as an entry deterrence strategy. Nevertheless Konigbauer (2007) does not assume the possibility raised by

[2] Brand name Prozac.

Gonzalez et al. (2006) of shifting demand to other molecules. The behaviors described have all it takes to undermine policies that depend on the consumers' sensibility to price, like RPS. In order to solve these problems, governments frequently try different strategies to control or suppress discretionary prescription from physicians. From restrictions to advertising, restriction on prescription by active ingredient (Kanavos et al., 2008 and Moreno-Torres et al., 2009), lists of available drugs to prescription, or dispenser permission to change prescription to the cheapest drug of the active ingredient (European Commission, 2009, Danzon et al. 2004), all has been tried to boost RPS' efficiency.

After its introduction, in Germany during the 90's, the use of this strategy has spread throughout Europe and in some other countries like New Zealand or the USA. However countries like United Kingdom, Norway, Austria or Sweden prefer to use economic evaluation as a way of setting reimbursement level[3]. On the other hand, some divergences might be sighted between the different schemes used in the adopting countries. Not intending to anticipate the discussion of the effects of those different schemes, we will expose the several approaches to the policy. Some countries like Belgium, France, Croatia, Portugal or Spain adopted the ATC-5[4] level of the WHO drug classification to cluster drugs. Others, like the Netherlands or Hungary used pharmacological class. Still others, use ATC-4 level, like Germany. A combination of classifications might be found in other countries, where depending on each cluster might use pharmacological class or active ingredient to group drugs.

Concerning the way the scheme defines the reference for reimbursement, numerous differences might be found in different countries. Croatia and Hungary define the reference as the mean of all prices. France uses the mean of all prices but only for generic drugs. A tighter scheme might be found in Finland, Italy or Spain where the reference is set equal to the lowest price of all drugs in the cluster. Someway close to the previous schemes is the one used by Denmark or Latvia that use the cheapest generic within the cluster. Portugal, in contrast, defines the reference as the mean of five cheapest generics inside the cluster since 2011. Even so, the most complex scheme might be found in Germany as a weighted mean of all drugs and calculated through regression analysis.

[3] Although it is outside the scope of the thesis, there is literature sustaining such option, see Drummond et al. (1997) "The role of economic evaluation in the pricing and reimbursement of medicines" Health Policy 40,199-205.

[4] According to ATC classification, level 1- Anatomical main group; level 2- therapeutic subgroup; level 3- Pharmacological subgroup; level 4- chemical subgroup; level 5- chemical substance.

Levels are increasingly stricter concerning the spectrum of drugs included.

The dynamic of the policy implementation is also interesting, Norway and Sweden actually adopted RPS in 1993, before dropping the measure during the last decade. Several other countries shifted from generic to therapeutic referencing. Italy and Hungary followed that path to return later to generic clustering. Finally Germany started by adopting therapeutic reference pricing, to abandon the measure for new drugs in 1996, and reintroduced it again in 2004 (Neeraj et al. 2009).

Such wide and differentiated use of the policy shows not only its malleability, but also the different utility functions of the policy makers. This way, we will address the effects of each particular design on the outcomes achieved.

2.2. Endogenous versus Exogenous RPS

As described above, there are several versions of RPS identifiable from the policies implemented worldwide. The classification we approach now depends on the ability of the firms in the market to influence the reference. Therefore, we can classify as endogenous or exogenous RPS.

The exogenous RPS is not a policy as popular as the endogenous version, and the reason might be on the lacking of incentives to trigger competition within the cluster. In fact, as described by Brekke et al (2011), in an exogenous system there is a clear incentive to converge to the reference price, after its reduction. Without the possibility of reducing the r, generic firms tend to increase the price as it is partly reimbursed. At the same time, with a cheaper competitor in the market, brand firms tend to decrease their price to avert the shifting of some demand to the generic. This way, we end up converging from above and from bellow r, and confirming the price convergence hypothesis.

Another approach on an exogenous RPS was made by Mestre-Ferrandiz (2003). Using a theoretical static model with two duopolists, a branded and a generic one, horizontally differentiated, the researcher reaches some different conclusions from Brekke et al. (2011). The author argues that the effects of RPS might depend on the level of r. In fact, within a certain interval of r, set by authorities, the RPS is able to induce price reductions for both drugs when compared to the simple reimbursement scheme. Even though the introduction of RPS might increase brand demand, overall expenditure is reduced, due to the price reductions previously

described. In the same paper the author finds profit reduction for both firms in the market. The different results found by these two studies might reflect the different assumptions made by the authors, since Brekke et. al. compare RPS to a market without regulation, whereas Metre-Ferrandiz et al. compare it to a pure reimbursement system.

Although there are few exogenous RP schemes in force, it is possible to imagine an endogenous RP that, in theory, could be closer to an exogenous one. A sort of hybrid RPS could be the one where the reference is set as a mean of the prices in a large cluster, and where the update of RP is set rarely. In that case, despite the fact that the reference could be defined inside the market, the decision of one firm hardly could change the reference. At the same time, the higher length of the period between updates leads to an increase of the payoff for generic firms, as a result of deviating from low prices. Thus, the study of exogenous RPS raises some interest despite the fact that it has been progressively dropped during the last decade in favor of endogenous RPS.

2.3 Endogenous RPS and Competition

The RPS is generally presented with one objective in the view of policy makers, to contain pharmaceutical expenditure, whether it comes from reducing reimbursements, or from the shift in demand to generics (Mestre-Ferrandiz, 2003). Indeed, the incentives to increase generics market share aim to restrict the pharmaceutical expenditure, specially the third payer share (Dylst et al. 2012). However, from the literature explored to perform this thesis, the least that can be said is that the reach of this goal, through this policy, is dubious (Kanavos et al., 2009). The literature consulted is consensual in one point, any kind of effect derived from this policy depends on the ability of the scheme built, to create or increase competition, within the generics drugs market, in each cluster and promoting financial responsibility among consumers (Lopez-Casasnovas and Jonsson, 2001; Ma, 1994; cit. by M. Miraldo, 2011). The focus put on competition is understandable in an endogenous system where the level of reimbursement is set as a function of the generic prices in the previous period:

$$r = \beta P_G + (1 - \beta) P_B, \tag{2}$$

where β (with $0 < \beta < 1$) defines the influence of each firm in r, in the following period. Despite being extracted from a model set for only two firms, it illustrates quite clearly that the

generic lower price exposes the branded price to a copayment. This effect is increased by what Ghislandi (2011) calls brand independence (BI) where β is set to 1 and the branded price has no influence in the construction of the reference price. This way, we assume that the generic firm is allowed to set the level of reimbursement freely. In its paper, dedicated to the influence of RPS on competition, BI holds a central role in its analysis. The author concludes that under BI, prices are always lower, than when BI does not hold (Ghislandi, 2011). In fact, the same author also recognizes that generic firms are "under the pressure of two opposite forces. One the one hand, the firms have an incentive to obtain a higher r, on the other hand, they do not want the branded to be close to the reimbursement level" (Ghislandi, 2011). Thus, it would be strategically profitable for generics to collude around r leaving it unchanged above their marginal cost. If that was the result of a RPS implementation, then, one might predict that r would be higher than optimal, prices paid by consumer would be lower for a sufficiently high reimbursement and consumption would be higher as well.

Merino-Castello (2003) approaches the theme comparing a market where consumers pay a fixed amount of drug price to a RPS. Using a vertical differentiated model with two firms, the author analyzes the RPS effects under Bertrand competition and under Stackelberg dynamic. Inspired by the introduction of the system in the Spanish pharmaceutical market, the researcher finds that after the insertion of the RPS all prices reduced. However, the effect is clearer on brand prices, although, under Stackelberg assumption, the brand market share increases. In fact, with the exception of Stackelberg results, the findings are in line with the literature. Nevertheless, the advantage of the brand, with the possibility of defining quantities might be an unrealistic one, since the pharmaceutical market seems more likely to compete in prices rather than in quantities.

The idea of the increase in competition after the introduction of RPS is also supported by Pavcnik (2002). Using data from Germany from 1986 to 1996, the author concludes that endogenous reference pricing actually increased price competition and forced brand drugs to reduce their price by 21% to 26% on average. Although reduction of prices for generics is less noticeable, it is increasing on the number of generics within the cluster. Another interesting point concluded by the author, which links us to the next point on this thesis, is that reimbursement reductions increase competition within the active ingredient group and not between therapeutic substitutes. Such result is particularly interesting since the German RPS clustering method is known to generate large clusters with several active ingredients within them.

Returning to Brekke et al. (2011), the empirical part of the work also suggests a clear effect of RPS. Using data for Norway from 2001 to 2004 for the 40 largest clusters, the authors conclude that there is a clear effect on prices. Thereby, Brekke et al. (2011) find a price reduction close to 30% of all drugs together with a substantial reduction in the brand market share. Looking at the scheme effects on the different kind of drugs, the data suggests that the effects on brand prices are stronger with 33% price reduction, than on generics with 22%. Concerning competition, the authors conclude that the number of generic competitors has a negative effect on the brand market share. On the contrary, the number of therapeutic competitors tends to increase the brand market share, what the authors justify with a previous price reduction in response to therapeutic competition that could improve that indicator.

It is now clear that the effects of this policy specially on public expenditure, but also for patients spending, can be strongly enhanced by triggering competition reducing generic prices to marginal cost, or at least closer to it. That kind of consequence provided by competition would decrease r turning brand drug more costly to patient shifting demand to generics and consequently forcing a reduction in the brand price, as proven by Brekke et al. (2011).

2.4. Therapeutic versus Generic RP

Obviously, the RPS is not applicable indiscriminately, usually each reference is attached to a cluster of drugs chosen for their therapeutic use or their active ingredient. Each cluster will have an own reference, set as each legislation determines, the lowest price inside the cluster, a mean of the cheapest prices as Portuguese present case, or the most expensive of the generic prices inside the cluster as it was in Portugal until 2010.

Brekke et al. (2007) describe three mechanisms of clustering the drugs; products with the same active chemical ingredients, products that may be neither chemically identical nor pharmacologically equivalent, but have comparable therapeutic effects. And finally, products with chemically related active ingredients that are pharmacologically equivalent. In this classification the authors define the first case as generic reference pricing. Implicitly, we are assuming that to have several producers of the same active chemical ingredient its patent must have expired. The second and third cases are defined as therapeutic reference pricing, in which, the cluster of drugs may include brand name under patent drugs. According to WHO's classification of drugs,

we could define a generic RP as the ATC-5 clustering method and therapeutic RP as ATC-4 clustering method. Such classification is often used in literature to describe both reference systems.

In fact, TRP schemes might include in the same cluster, and at the same time, under patent drugs, off patent drugs and generic drugs. Although this distinction refers to very little details that might seem innocuous at the first sight, the difference between them has been raising some controversy inside the pharmaceutical industry and scientific community. The main argument for the controversy is whether patent drugs should be subjected to competition during its patent protection period or not and the effects that competition might have on the stimulus for R&D from pharmaceutical companies.

The policy makers' option for one version of RP is not indifferent to the objectives intended for the pharmaceutical market. There is a broad spectrum of decisions when we analyze international RPS. New Zealand, the Netherlands and Germany opted for the therapeutic version of the policy (Danzon et al, 2004). Other countries like USA, Spain and Portugal, however, have chosen the generic version (Danzon et al, 2004, Moreno-Torres et al. 2009).

The different options in those countries raise the question of what drove decision makers to opt for one version instead of the other. Brekke et al. (2007) used a theoretical approach on the theme. The model developed assumes three firms, one of them still under patent protection, and two others, one generic, and one of the branded without patent protection. The authors also assume that the branded drugs are horizontally differentiated, while there are high quality consumers and low quality consumers (brand and generic consumers respectively). The authors conclude that generic RP should never be considered as this version tends to increase the total mismatch costs of drugs[5]. This version of RP is also known to create what is described as "generic paradox". This phenomenon happens when after the entry of a new generic in the market, it is possible to observe an increase in the price charged by the branded drug. The propensity for the generic paradox is related to generic RP as it creates a gap between the prices, paid by the patient, for the two drugs, since the under patent drug is not reimbursed at all. This fact implies that the branded drug only keeps the more insensitive consumers, which triggers an incentive to increase price. Implicitly, we are talking of a cross effect since the patent drug is not on the system and can only be affected by some kind of substitutability with the generic versions

[5] In this approach, consumers face a cost of deviating from their natural choice, that is the closest firm in the demand space. See Brekke et al. (2007)

available in the market. Either way, more important to the theme discussed here is the fact that "the competitive effect of TRP is larger in markets where there is less competition to begin with. This suggests that, if the regulator is mainly concerned about reducing drug spending, the therapeutic clusters should be broadly defined" (Brekke et al., 2007).

The previous idea of increased competition in broader clusters goes in line with the conclusions derived by Danzon and Ketcham (2004). The authors explore the applicability of TRP in Medicare through the experience of countries such as Germany, Netherlands and New Zealand. From the comparison of the different systems, the authors conclude that the broader clusters of the German system allowed the country to benefit from lower prices and consequently lower reimbursements from the public system. However, that benefit achieved had a large cost given by reduction in new drugs entry to the market.

Even though the price reduction caused by the introduction of RPS might be more aggressive in the therapeutic version, GRP also induces brand price reductions. That idea is supported by Bergman et al. (2003) in a study on the potential competition in pharmaceutical markets. Using data from eighteen pharmaceutical substance markets in Sweden, the authors conclude that the introduction of GPS decreased brand prices facing generic competition by 14 to 15%. Nonetheless, later generic entrants seem not to have the same price decreasing effect they had before the introduction of the policy. This seems to indicate that price reductions caused by RPS happen right after patent protection expiration and with the first generics entries to the clusters. Using data for the same country from 1972 to 1996, but with only twelve molecule markets, Aronsson et al. (2001) reach some similar conclusions. The introduction of reference pricing managed to increase generic market shares in five markets and reduced pharmaceutical prices specially of branded drugs. Simultaneously, the number of generics within the cluster increased the relative difference between brand and generic prices. Those results are in line, not only with Bergman et al. (2003), but also with Puig-Junoy (2010) and seem to gather some consensus on the particular effect of GRP on brand prices and its dependency on generic competition to reach a higher effect.

Concluding the analysis on the dichotomy therapeutic versus generic RP, broader clusters increase competition, reducing pharmaceutical costs (Brekke et al., 2007). In this case, TRP produces more containment by including brand and patent protected drugs in the system. However, the expenditure reduction and a broader cluster also reduce the incentives to new

entry. Concerning market entry and investments in R&D, literature addresses effects in an isolate fashion, which is somehow an unrealistic approach as effects from the cluster structure of RP (whether generic or therapeutic) and the source of reference (endogenous or exogenous) often intersect as most countries policies are hybrid.

2.5. R&D and market entry.

New market entries, of innovative drugs, are an issue of concern for health policy decision makers. In fact, innovations in health procedures often come from three different areas, new diagnostic techniques or procedures, new chirurgical techniques and new pharmacological treatments. While diagnostic and chirurgical techniques are easily and quickly adopted by surgeons, pharmacological innovations depend on market conditions to enter a specific country. Admitting that a specific health system will be deprived of a new treatment for several years, because of the market regulation of the country has health, social and political costs. We are facing here a tradeoff between today's costs and fewer new treatments in the future for growing populations (Neeraj et al. 2009). Thus, the discussion of what influences market entry and R&D investments is of some interest.

The R&D issues are addressed by Bardley et al. (2009) using a theoretical approach. The authors use a dynamic model with three agents - pharmaceutical firms, consumers, and a regulatory entity. In the end, the instigators test the influence of model variables with an empirical work on the French market of statins. The study concludes that the reference pricing scheme tends to delay new innovations since the threat of generic competition, after losing patent protection, reduces future revenues. Still, generics on their hand have to consider the effects of price competition when entering the market. Under authors considerations, this threat might delay competition and by so, increase incentives to launch pioneers (Bardley et al., 2009). Another interesting point on this issue is the increased incentives that therapeutic RP creates to new breakthrough innovations. As the so called me-too drugs tend to be introduced in existing clusters, under price competition, pharmaceutical firms try to avoid that competition by creating new treatments (Bardley et al., 2009).

The distortions raised by price regulations do not affect only R&D investments. The market entry of innovative drugs might be delayed in countries that limit firms natural pricing strategies. Kyle (2003) explores the idea with an empirical paper using data for all drugs

developed between 1980 and 2000 and respective date of market entry crossed with OECD health data set. The author reaches some interesting conclusions concerning market entry and diffusion of drugs through markets. Countries with strict regulatory policies tend to see delays in the entry of new drugs in their markets. Consequently, these countries tend to be the last receiving innovative drugs. The launch of a drug in countries like France, Italy or Spain reduces the probability of introducing the same drug in other markets. Furthermore, if those remaining countries also have price controls, the probability of entry reduces by another 15-25%. At the same time, drugs developed by American, British and Swiss firms reach more countries than French, Italian or Japanese firms, which might be related with the regulatory policy used by the firm's country of origin. Curiously, firms from countries without price regulation tend to avoid countries that use such policies, which might function as a protectionist strategy (Kyle, 2003).

Although without the serious concerns related with health and innovative treatments exposed above, generic entry has gained importance in economic literature. Generic entry has deep influence in the RP scheme outcomes. Gishlandi et al. (2005) conclude that Italian RPS could derive higher welfare if there were a higher number of generic competitors within the clusters. Thus, it is no surprise that policy makers often face a narrow window of decision. On one hand, they are interested in generic competition and in squeezing pharmaceutical market margins; on the other hand they are interested in generic entry and higher incentives to its consumption. Moreno-Torres et al. (2009) explore generic entry determinants using Spanish data on 77 active ingredient markets from 1999-2005. The authors conclude that revenues, market age, and more surprisingly, brand competitors have positive effect on generic market entry. The answer to the apparent paradox of increased generic entry in markets with more brand competitors might lie on molecule market size. Bergman et al. (2003) argues that larger market size increases generic entry and brand firms might be also attracted by the same reasons generic firms are. Thus, market size may induce higher revenues which invite both brand and generic competitors. On the other side, the number of generic incumbents and regulation reduce generic entry (Moreno-Torres et al., 2009). The authors conclude that the introduction of RP in Spain in 2000 reduced the number of new generic entries by 48% and the new version of the system introduced in 2004 reduced the amount of new entries by another 72%[6] (Moreno-Torres

[6] The authors use a negative binomial regression, and due to the large number of zeros created by the markets where there was no generic entry in several quarters, also use a zero-inflated negative binomial regression. All independent variables are statistically significative. Generic imbumbents in the market reduce expected number of entries by 5,65%, for each additional brand competitor the average number of entries increase 9,97%. For each

et al., 2009). The European Commission (2009) reached the same conclusion, for tightly regulated markets, generic entry tends to diminish and to delay in time. However, some regulatory policies, like compulsory generic substitution by pharmacists, tend to increase generic entry.

The incentive to price reduction might be specially dangerous when it comes to R&D. Reduction in R&D investment might be the optimal strategy for a firm if new investments do not deviate it from competition. In that case, the new drug would be included in a cluster exposing the investment to a low return. As a consequence of the hard competition, fewer innovative drugs would enter the market, exposing consumers to the cost of not having the ideal drug for the treatment they need.

million euros increase in revenues, the average generic entries increase 3.6%. And finally, for each quarter since the first entry the expected number of entries reduces in 20,10% (Moreno-Torres et al. 2009).

3. The Model

To approach this theme in an analytical fashion, we model a market of an off-patent prescription drug. That way, issues concerning R&D developed in the literature review are disregarded. From the demand side, we have n consumers uniformly distributed on a line of length one. For simplicity we normalize n to 1. Each consumer demands one unit of the prescribed drug.

From the supply side we have three firms within the cluster, one branded (B) and two generic firms that we will call generic 1 (G1) and generic 2 (G2). In order to describe the market we use a derivation of the Hotelling model where the three firms are located in the line[7]. Generic 1 drug is located at point zero, and generic drug 2 is located at l<1, so that it captures a bigger share of the demand for the prescription drug, all else equal[8]. The location of the generic 2 drug is intended to imply the price difference among the generic drugs required to analyze the policy implications of a shift in the price weights of the reference system. The branded drug, however, does not have a "physical" location within the line. That way, consumers along the line homogeneously perceive the branded drug quality, or characteristics, to be the same[9].

The utility of the consumer located at x and consuming one unit of the drug from one firm (j) might then be defined as:

$$U(x,j)\begin{cases} U - C_B & if\ \ j = B \\ U - C_{G1} - tx & if\ \ j = G1 \\ U - \ C_{G2}\ - t|l - x| & if\ \ j = G2 \end{cases}; \qquad (3)$$

Where x is the location of the consumer in the line, U is the utility derived from the consumption of the drug. So, C_B, C_{G1} and $C_{G2,}$ are respective copayments. Finally, the parameter t is the marginal cost of travelling along the line. Although this parameter is not crucial for the analysis, it deserves some considerations. It captures the level of vertical differentiation and therefore, the advantage of the branded firm since its consumers do not face those costs. Thus, one can intuitively predict that a higher t increases brand market share and for that reason its price, but most of all, reduces the competition effects triggered by the reference pricing scheme. Yet, t also

7 Unlike Harold Hotelling (1929) firm location refers to the tastes of consumers and not to physical locations.

8 Further ahead in the thesis, we will impose a restriction on / values in order to guarantee a stable Nash equilibrium.

9 Equivalent to assuming that the branded drug is located at each point on the line.

captures the level of horizontal differentiation between generics, like in the classical Hotelling model[10]. Consequently, t captures both differentiation effects.

In a market with insurance intervention, the consumer gets to pay only a part of the real price of the drug. Like it is expressed in the utility function (4), the share supported by the consumer may be called the copayment and is the only portion of the price relevant for the consumer decision. Assuming that $P_{G1} < P_{G2} < P_B$ copayment might also be endogenously defined as:

$$C_B = \alpha r + P_B - r, \tag{4}$$

$$C_{G1} = \alpha P_{G1}, \tag{5}$$

$$C_{G2} = \alpha r + P_{G2} - r, \tag{6}$$

where $\alpha \in (0,1)$ is the coinsurance rate; P_B, P_{G1} and P_{G2} are respectively the brand, generic 1 and generic 2 firm prices, and r is the reference price. From the function exposed above, it is straightforward to realize that a market with no regulation could be a particular case of the model described if we set $\alpha = 1$. That way, the consumer would pay the price of the drug without any reimbursement.

Concerning the reference price (r) we use an approach similar to the one used by Brekke et al. (2011), with the reference set as a function of market prices, however, in this function, both prices are from generic drugs. That way, the model is able to endogenize r:

$$r = \beta P_{G1} + (1 - \beta) P_{G2}, \tag{7}$$

where $\beta \in (0,1)$ is the weight of generic 1 price in the reference used for reimbursement.

Since we have defined utility function and all the endogenous variables of the model, we can now derive the indifferent consumers between either the generic 1 drug and the brand, and the brand and generic 2 drug. To derive the indifferent consumer locations we have to equalize utility functions of brand consumers and generic firm 1 consumers:

$$U - C_B = U - C_{G1} - tx, \tag{8}$$

Solving for x and replacing C_B and C_{G1} for the respective functions (4) and (5) we get the expression for the location of the indifferent consumer (z_1):

[10] In the classical Hotteling model transportation costs have a literal interpretation. However, the higher t increases the cost of traveling the same distance. See Harold Hotelling, "Stability in Competition"(1929)

$$z_1 = x = \left(\frac{\alpha r + (P_B - r) - \alpha P_{G1}}{t}\right). \quad (9)$$

Using the same methodology, but this time for the upper indifferent consumer, we have the equality of the utility derived from the consumption of the branded drug and generic 2 drug is given by:

$$U - C_{G2} - t(l - x) = U - C_B. \quad (10)$$

Once again, solving for x and replacing C_B and C_{G2} for (4) and (6) respectively:

$$z_2 = x = l - \left(\frac{P_B - P_{G2}}{t}\right), \quad (11)$$

where z_2 is the indifferent consumer between the brand and the generic 2.

With the expressions of indifferent consumers setting the bounds of each firm market, we might define demand functions for each firm as:

$$y_B = z_2 - z_1 \quad ; \quad y_{G1} = z_1 \quad ; \quad y_{G2} = 1 - z_2, \quad (12)$$

where y_B, y_{G1}, y_{G2} are respectively brand, generic 1 and generic 2 firm demands. Replacing (11) and (9) in (12) we explicitly define demands as:

$$y_B = l - \left(\frac{\alpha(r - P_{G1}) + (2P_B - r) - P_{G2}}{t}\right), \quad (13)$$

$$y_{G1} = \left(\frac{\alpha r + (P_B - r) - \alpha P_{G1}}{t}\right), \quad (14)$$

$$y_{G2} = 1 - l + \left(\frac{P_B - P_{G2}}{t}\right). \quad (15)$$

To illustrate the market described above, consider the following figure:

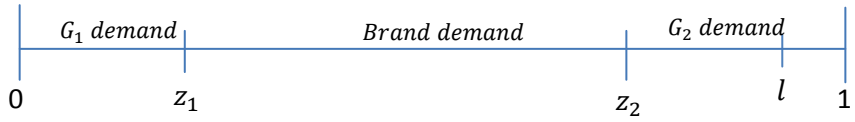

Figure 1

In order to simplify the model no variable or fixed costs of production are assumed. Although it is not the case of innovative drugs, the previous assumption is not that far from reality, since new generic competitors and brand incumbents face very reduced costs of production in most molecules. So, profit functions become price times demand as follows:

$$\pi_B = P_B y_B \quad ; \quad \pi_{G1} = P_{G1} y_{G1} \quad ; \quad \pi_{G2} = P_{G2} y_{G2}; \quad (16)$$

where $\pi_B, \pi_{G1}, \pi_{G2}$ are respectively brand, generic 1 and generic 2 firm profits. The subsequent game assumes the following rules - first the policy maker defines the drug price share supported by the consumer and the weight of each generic in the reference. Then, the three firms play a simultaneous pricing game.

3.1 Nash equilibrium

Using profit functions defined at (16) and replacing demands for (13), (14) and (15), respectively, we end up with profit expressions as functions of prices and the reference. Taking first order conditions in order to optimize profits, and solving for each price we get best response functions;

$$P_B(P_{G2}, P_{G1}) = \frac{\left((2-\mu)P_{G2}+\mu P_{G1}+lt\right)}{4}, \quad (17)$$

$$P_{G1}(P_0, P_2) = \frac{(P_B-(1-\mu)P_{G2})}{2\mu}, \quad (18)$$

$$P_{G2}(P_B) = \frac{\left(P_B+t(1-l)\right)}{2}, \quad (19)$$

where μ is a parameter, increasing in either α or β as follows:

$$\mu = \alpha + \beta(1-\alpha) \;\; ; \quad \mu \in (0,1). \quad (20)$$

At this point, we are able to develop the first interpretations from the model. As it is possible to understand from best response functions, prices are strategic complements. The exception here is the relation between P_{G1} and P_{G2} that is of strategic substitutes, although P_{G2} does not depend on P_{G1}.

The interesting point here is not only the fact that generic prices are the exception by being strategic substitutes, but also that they do not have the same impact on each other. Looking at them separately, the effect of a price increase of P_{G2} decreases P_{G1}. The clue to the explanation of this outcome might be implicit in the reference pricing. The reader could note that the strength of this substitution effect depends on μ. In fact, an increase in P_{G2} increases r, if μ is not set equal to one ($\mu = 1$)[11]. The increase of r reduces copayment from branded drug (C_B), all

[11] Means that P_{G2} has some influence in r. If $\beta = 1$ or $\alpha = 1$ then $\mu = 1$ and from the equation (12) the effect of P_{G2} on P_{G1} is null.

else equal. In its turn, the reduction of the copayment increases brand demand since the branded drug becomes relatively cheaper. Finally, the brand demand increase shifts the location of the indifferent consumer (z_1) to the left, reducing generic firm 1 demand and obliging the firm to answer reducing prices.

The opposite, though, is not true. An increase in P_{G1} has no effect on P_{G2}. Once again the reason is r. An increase in firm 1 price raises r, hence, reducing copayment for the branded drug. Unlike the previous description, this time, the shift in r also affects the generic drug in the same amount it affects the branded drug's price. This way, the relative prices for consumers remain the same, leaving the location of the indifferent consumer unchanged. Therefore, the demand for the second generic, as well as its price does not change, all else equal. Indeed, the expression "all else equal" gains substantial emphasis in this case. Although P_{G2} has a negative direct effect on P_{G1}, and P_{G1} has no direct effect on P_{G2}, they do have indirect contradictory effects through P_B. The positive effect of an increase of P_{G2} on P_B is more than proportional for any $\mu < 1$, and that strategic complement effect is transferred through the brand price to P_{G1}. The same happens with the effect of P_{G1} on P_B, and once again, through it, on P_{G2}. With this information, economic intuition tells us that a decrease in one price should led to general decrease of all prices, even with the exceptions described above.

Simultaneously solving first order conditions in order to find equilibrium prices we get:

$$P_B = t\left(\frac{(3+l-(1-l)\mu)}{11+\mu}\right) \;;\; P_{G1} = t\left(\frac{3l-2+(3-2l)\mu}{11\mu+(\mu)^2}\right) \;;\; P_{G2} = t\left(\frac{7-5l}{11+\mu}\right). \quad (21)$$

Thus, firms demands become:

$$y_B = \frac{2(l+\mu(l-1)+3)}{\mu+11} \;;\; y_{G1} = \frac{3l+\mu(3-2l)-2}{\mu+11} \;;\; y_{G2} = \frac{7-5l}{\mu+11}; \quad (22)$$

and respective explicit profit functions:

$$\pi_B = 2t\left(\frac{l+\mu(l-1)+3}{\mu+11}\right)^2 \;;\; \pi_{G1} = t\,\frac{(3l+\mu(3-2l)-2)^2}{(\mu)(\mu+11)^2} \;;\; \pi_{G2} = t\left(\frac{5l-7}{\mu+11}\right)^2. \quad (23)$$

In order to produce a Nash equilibrium that respects the conceptual model described above, we introduce some conditions that restrict the set of values that one or more variables might assume. Above all, we need to guarantee that generic firm 1 is always the less expensive drug in the market. Such condition enables the reference system to fluctuate between generic prices.

Assumption 1: In equilibrium generic firm 1 drug is always the cheapest drug available for consumers.

This assumption grants that there is a price gap between the two generic firms with the purpose of allowing the reference scheme to shift the weight between them both. So analytically we have $P_{G1} < P_{G2}$ and then:

$$t\left(\frac{3l-2+(3-2l)\mu}{11\mu+(\mu)^2}\right) < t\left(\frac{7-5l}{11+\mu}\right). \quad (24)$$

The previous inequality (24) is satisfied for any $l < \left(\frac{2(1+2\mu)}{3(1+\mu)}\right)$ and in that case, it is clear that for $\mu = 1$, which is true for $\alpha = 1$ or $\beta = 1$, any l in the market produces a $P_{G1} < P_{G2}$. The exception here is the extreme point $l = 1$, where the game between the two firms becomes symmetric and then $P_{G1} = P_{G2}$. For $\mu = 0$, value that may be achieved for $\alpha = 0$ or $\beta = 0$, the set of locations that fulfills this condition is reduced to $0 < l < \frac{3}{4}$.

Assumption 2: In equilibrium all demands are positive.

This grants that all firms produce in equilibrium. So, for firm 1 we have;

$$z_1 = \frac{3l-2+(3-2l)\mu}{\mu+11} > 0, \quad (25)$$

that is satisfied for $l > \frac{2-3\mu}{3-2\mu}$.

For firm 2 the previous assumption assumes the form of the condition:

$$1 - z_2 = \left(\frac{7-5l}{\mu+11}\right) > 0, \quad (26)$$

which is satisfied for any $l > -\left(\frac{\mu+4}{5}\right)$, and then for all $l \in [0,1]$.

The brand demand must also be positive which means,

$$z_2 - z_1 = \left(\frac{2(3+l-\mu+l\mu)}{\mu+11}\right) > 0, \quad (27)$$

and may be satisfied if $l > \frac{\mu-3}{1+\mu}$, and once more for all $l \in [0,1]$ meaning that concerning the demand, the branded firm and the generic firm 2 have positive demands in equilibrium for any l. Concluding, the second assumption of the model only implies the restriction for the positivity of firm 1's demand, and therefore, $l > \frac{2-3\mu}{3-2\mu}$ in equilibrium.

Assumption 3: The location of the indifferent consumer between the branded drug and the generic 2 drug is to the left of[12] l in equilibrium ($z_2 < l$).

$$l - z_2 = l - \left(\frac{5l+4+\mu}{\mu+11}\right) = \frac{(6l-4-(1-l)\mu)}{(11+\mu)} > 0, \quad (28)$$

is satisfied if $l > \frac{4+\mu}{6+\mu}$. Reminding the conclusions of assumption 1 and 2, this restriction diminishes the set of locations available for a stable equilibrium, binding assumption 2 and the same for the assumption that $P_{G2} < P_B$.

Assumption 4: All consumers located in the interval $]z_2, 1]$ prefer G_2 over B.

The assumption is satisfied if the following condition is true;

$$l - z_2 \geq 1 - l, \quad (29)$$

$$l \geq \left(\frac{15+2\mu}{17+2\mu}\right). \quad (30)$$

Since,

$$\frac{2\mu+15}{2\mu+17} - \frac{4+\mu}{6+\mu} = 2\left(\frac{\mu+11}{2\mu^2+29\mu+102}\right) > 0; \quad (31)$$

the assumption 4 binds previous assumptions 2 and 3 and decreases substantially the set of locations available for a stable equilibrium.

The equilibrium requires that all conditions are fulfilled, and so, from assumption 1 and 4;

$$\frac{15+2\mu}{17+2\mu} < l < \frac{2(1+2\mu)}{3(1+\mu)}. \quad (32)$$

The parameter space defined by (32) is non-empty if:

$$\frac{2(1+2\mu)}{3(1+\mu)} - \frac{15+2\mu}{17+2\mu} = \left(\frac{2\mu^2+21\mu-11}{6\mu^2+57\mu+51}\right) > 0 \Rightarrow \mu > \frac{1}{2}. \quad (33)$$

We can now conclude that there is a set of locations and μ values that satisfy all the conditions and may generate a stable equilibrium. For α =1 or β =1 then $\mu = 1$ resulting in

[12] Graphically is to the left of /as can be seen in figure 1.

$\frac{17}{19} < l < 1$. We then end with an upper and a lower bound of locations where a stable equilibrium is possible and that come from a function of α and β:

$$l \in (\underline{l}(\alpha, \beta), \bar{l}(\alpha, \beta)). \quad (34)$$

3.2. Comparative statics

Now that we know the locations available for equilibrium, we can use the expressions exposed to describe the model, in order to derive conclusions about profits, prices, market shares, consumer utility and third payer share. Beginning with prices and taking the derivatives of the expressions for equilibrium prices, with the purpose of studying the effect of a change in the coinsurance rate (α) and in the weight of the different generics on reference scheme (β), on firm prices, we get;

For the branded firm;

$$\frac{\partial P_B}{\partial \alpha} = -2t(\beta - 1)\left(\frac{5l-7}{(-\mu-11)^2}\right) < 0, \quad (35)$$

$$\frac{\partial P_B}{\partial \beta} = -2t(\alpha - 1)\left(\frac{5l-7}{(\mu+11)^2}\right) < 0. \quad (36)$$

For generic firm 1;

$$\frac{\partial P_{G1}}{\partial \alpha} = -t(\beta - 1)\left(\frac{22+(\mu)(4-3\mu)+2l(-\mu)(3-\mu)-33l}{\left((-\mu-11)(-\mu)\right)^2}\right) < 0, \quad (37)$$

$$\frac{\partial P_{G1}}{\partial \beta} = -t(\alpha - 1)\left(\frac{22+(\mu)(4-3\mu)+2l(-\mu)(3-\mu)-33l}{\left((-\mu-11)(-\mu)\right)^2}\right) < 0. \quad (38)$$

For generic firm 2:

$$\frac{\partial P_{G2}}{\partial \alpha} = -t(\beta - 1)\left(\frac{5l-7}{(\mu+11)^2}\right) < 0, \quad (39)$$

$$\frac{\partial P_{G2}}{\partial \beta} = -t(\alpha - 1)\left(\frac{5l-7}{(\mu+11)^2}\right) < 0. \quad (40)$$

All the partial derivatives are negative for any location within the set able to produce equilibrium, as described above. This finding goes in line with the literature analyzed in previous chapters, and tells us that an increasing coinsurance rate, as well as an increasing weight of the cheapest generic on the reference implies a general price reduction. Although the effect and part

of the mechanism might be the same, the reasoning for such effect is different for the two parameters.

The outcome of a coinsurance increase might be explained by the increased exposure of consumers to prices. This way, consumers become more sensitive to the price differences between drugs, once without any price change branded drug becomes relatively more expensive. The previous description configures a price elasticity increase caused by the reduction of the share covered by the third payer. If that is true, then firm 1 has higher incentives to trigger a price war, since for the same price reduction the demand share captured is bigger. This precise effect will be checked when analyzing demand effects of a variation of α.

When it comes to the effect of a fluctuation in the influence of the cheapest generic (β) on prices, the results also indicate a general decrease of prices. With the increased influence of its price, firm 1 has incentives to reduce it, exposing the other firms' consumers to a growing copayment of their drugs. Once again, reference pricing raises the incentives to trigger price competition through the increase in price elasticity of demand. Following this price strategy from firm 1, the other firms on the market are obliged to react trying to save their demands, and in such a market, that can only be achieved through a price reduction. The difference between parameters here (α and β) is in the onus of triggering the price demand elasticity increase. The change in α produces a direct effect of the policy maker decision, however, the change in β allows generic firm 1 to have that influence.

Proposition 1: An increase in the coinsurance rate or in the relative weight of the cheapest generic on r, leads to a general price decrease.

To complete the comparative statics analysis of prices is crucial to analyze the effects on firm demands for the same parameters. Regarding the demand we get the following results.

For the Branded firm;

$$\frac{\partial y_B}{\partial \alpha} = -4t(\beta - 1)\left(\frac{5l-7}{(\mu+11)^2}\right) < 0 \quad ; \quad \frac{\partial y_B}{\partial \beta} = -4t(\alpha - 1)\left(\frac{5l-7}{(\mu+11)^2}\right) < 0. \quad (41)$$

For Firm 1;

$$\frac{\partial y_{G1}}{\partial \alpha} = 5t(\beta - 1)\frac{5l-7}{(\mu+11)^2} > 0 \; ; \; \frac{\partial y_{G1}}{\partial \beta} = 5t(\alpha - 1)\left(\frac{5l-7}{(\mu+11)^2}\right) > 0. \quad (42)$$

For firm 2;

$$\frac{\partial y_{G2}}{\partial \alpha} = -t(\beta - 1)\left(\frac{5l-7}{(\mu+11)^2}\right) < 0 \quad ; \quad \frac{\partial y_{G2}}{\partial \beta} = -t(\alpha - 1)\left(\frac{5l-7}{(\mu+11)^2}\right) < 0. \qquad (43)$$

Following the price effects explanation, the demand's first order derivatives in order to α and β, expressed above, not only support, but also complement the analysis of the market. Looking at the expressions, it is clear that an increase in either parameter under study increases firm 1's demand, diminishing firm 2's and Brand's demand. This information suggests, once again, that the price reduction of the two latter firms happens precisely in response to this demand reductions. At the same time, the demand increase for firm one's drug is due to the price reduction fostered by the change in parameters. Concluding, when looking at demand effects we are looking at derivate effects of the price changes. These results are in line with Aronsson et al. (2001), explained in the literature review, since the introduction of RPS increased generic market shares.

Proposition 2: An increase in the coinsurance rate or in the relative weight of the cheapest generic on r raises the cheapest generic market share and reduces the brand and expensive generic share. The generic market share, as a whole, increases.

Now shifting the focus to firm profits, for the brand firm;

$$\frac{\partial \pi_B}{\partial \alpha} = -8t(\beta - 1)\left(\frac{5l-7}{(\mu+11)^3}\right)(l - \mu + l\mu + 3) < 0, \qquad (44)$$

$$\frac{\partial \pi_B}{\partial \beta} = -8t(\alpha - 1)\left(\frac{5l-7}{(\mu+11)^3}\right)(l - \mu + l\mu + 3) < 0. \qquad (45)$$

For firm 2,

$$\frac{\partial \pi_{G2}}{\partial \alpha} = 2t(\beta - 1)\left(\frac{(5l-7)^2}{(\mu+11)^3}\right) < 0 \quad ; \quad \frac{\partial \pi_{G2}}{\partial \beta} = 2t(\alpha - 1)\left(\frac{(5l-7)^2}{(\mu+11)^3}\right) < 0. \qquad (46)$$

In order to simplify the analysis of profits, and due to the complexity of the expression for firm 1's profits, the expression is evaluated at $\beta = 1$ and $\alpha = 1$. This adaptation in the approach implies a slightly restrictive analysis. In fact, unlike all previous interpretations the results obtained are obviously valid at points $\beta = 1$ and $\alpha = 1$ only. So, for firm 1;

$$\left.\frac{\partial \pi_{G1}}{\partial \beta}\right|_{\beta=1} = -t(1 - \alpha)\left(\frac{31l^2+2l-29}{864}\right) \quad ; \quad \left.\frac{\partial \pi_{G1}}{\partial \alpha}\right|_{\alpha=1} = -t(1 - \beta)\left(\frac{31l^2+2l-29}{864}\right). \qquad (47)$$

For generic firm 2, and for the brand firm, the effects on profits are quite clear, they decrease for an increase of both parameters. This effect is obvious since we had seen that both demand and prices were decreasing in α and β. Those two combined effects could only result in a profit decrease. Concerning firm 1, the outcome is a bit more complex. From expressions above, we can understand that all depends on the second degree polynomial in the numerator. The root acceptable within the model is $l = \frac{29}{31}$ meaning that firm one's profit depends on the level of horizontal differentiation assumed. If the firm 2's location assumed in the market is bigger than the previous value, say $l > \frac{29}{31}$, then generic 1 firm profits decrease. However, if the level of horizontal differentiation is lower, say $l < \frac{29}{31}$, firm one's profits will increase.

The basis behind such outcome is related to the balance between demand increase and price decrease. The closer firm 2 is to the middle of the market, the lower brand price might be. This effect implies a smaller dispersion of prices between the three firms, which means that for the same price reduction from firm 1's side, yields a smaller demand increase. This reduction in price elasticity of demand, forced by the lower value of l, decreases the profitability of the price reduction, and for a location sufficiently close to the center of the market, the effect of a increase of β or α becomes negative for generic firm 1.

Proposition 3: An increase in the coinsurance rate or in the relative weight of the cheapest generic on r, reduces the profits of the brand and the expensive generic firm. The effect on the cheapest generic firm profits depends on the degree of horizontal differentiation.

4. Welfare analysis

The welfare analysis is probably the most important part of this entire thesis. Taking a philosophical perspective on the subject, welfare is a measure of the value generated by market transactions between agents. Such concept means that we are interested in understanding the implications of policy shifts, on overall value created, and also on the value that each agent extracts from the market.

We are now able to reach the core of the project and interpret the political implications of the pharmaceutical reference pricing scheme. In order to achieve this objective, we will take a closer look at the three components of total welfare, these being total utility, total profits and third payer's share, in this precise order. To finish, we will evaluate the effects on the aggregate entity, total welfare and total welfare minus profits. Unlike the methodology used up to this point, I will drop the study of rate of coinsurance (α), to focus completely on the effect that a change in the influence of the cheapest generic on the reference scheme (β) has on each component of welfare.

4.1. Total Utility

Starting with total utility, this entity has four components, the utility of the firm 1's consumers, from brand's consumers and finally from firm 2's consumers. The generic 2 consumers might be divided in two groups, completing the four sections referred, the utility of consumers below l of firm 2 and those above firm 2's location. Reminding the utility function of firm 2's consumers, the module captures precisely the two shares of the second generic drug's demand. Therefore total utility (Q) becomes;

$$Q = \int_0^{z_1} (U - C_{G1} - ts)ds \quad + \int_{z_2}^{l} \big(U - C_{G2} - t(l - s)\big)ds \quad +$$

$$\int_l^1 (U - C_{G2} - t(s - l))ds + (z_2 - z_1)(U - C_B). \tag{48}$$

Taking first order derivative and evaluating at point $\beta = 1$ we obtain;

$$\left.\frac{\partial Q}{\partial \beta}\right|_{\beta=1} = -t\left(\frac{(1-\alpha)\big((7-5l)(31-5l)+ 6\alpha(23-37l)\big)}{864}\right) \gtrless 0. \tag{49}$$

The previous expression tells us that the effect of a slight reduction in β, when the reference scheme sets all the weight on the cheapest generic, is ambiguous. For a sufficiently high value of coinsurance, say α near 1, the effect of a reduction in β, when the parameter is set equal to 1 reduces total utility. Remember that for $\alpha = 1$ this derivative holds no significance, since for that value of coinsurance we end in a market with no reimbursement and thus with no influence for r. From an analytical perspective, for a lower α, the location required to turn the expression (49) to negative terms is higher. When $\alpha \leq \frac{13}{21}$ the expression assumes negative values for any l inside market bounds, meaning that a reduction of β would increase consumer utility. The economic justification for such result might be explained through the brand price. A decrease in β implies an increase in r since the expensive generic gains weight in the r function. As a consequence, the branded drug becomes relatively cheaper for the consumers and that effect increases their utility. Yet, drug prices increase as we could verify in the previous section, and that reduces total utility. Consumers then face two contradictory effects, but if α is sufficiently low, the first one always dominates. When $\alpha \leq \frac{13}{21}$, consumers get to pay a small share of the real drug price. Consequently, the general price increase that comes from the reduction of β has little effect on consumers.

Nevertheless, it is important to underline the effect of l and t in this expression. The level of horizontal differentiation of generics (t and l) increases function value and thus amplifies the utility reduction or increase effect of deviating r from generic drug 1.

Proposition 4: A marginal reduction in the relative weight of the cheapest generic on r, when $\beta = 1$, has ambiguous effects on consumer's utility, it depends on α. For $\alpha \leq \frac{13}{21}$ consumer's utility increases, for $\alpha \geq \frac{13}{21}$ utility might decrease.

4.2. Total Profits

For total profits the effects are quite intuitive. The expression of the aggregate is rather simpler and intuitive than total utility, consisting on the sum of all profits from market firms, in equilibrium. As a nomenclature simplifying procedure we will call it J;

$$J = P_1 y_1 + P_2 y_2 + P_0\big(1 - (y_1 + y_2)\big) = t\left({y_2}^2 + \frac{{y_1}^2}{\mu} + \frac{{y_0}^2}{2}\right). \quad (50)$$

Taking first order derivative of the function, and assuming the same conditions $\beta = 1$;

$$\left.\frac{\partial J}{\partial \beta}\right|_{\beta=1} = -t\left(\frac{(1-\alpha)(19-(13-4l)l)}{216}\right) < 0. \quad (51)$$

Now the result is substantially clearer. A small reduction of β, once again, in other words, a small increase in the influence of the expensive generic, increases profits of the firms in the market, as an aggregate. Recalling the result of the static analysis on individual profits, we know that generic firm 1 may increase or decrease profits depending on the level of horizontal differentiation, and the other two supply players reduce their profits on the increase of β. What this result adds to this analysis is that the increase from firm one is more than compensated by the decrease of the other two firms.

Proposition 5: A marginal reduction in the relative weight of the cheapest generic on r, when $\beta = 1$, increases total profits of the industry.

4.3. Third-payer's expenditure.

Extending the study to the third-payer's expenditures, which is the amount between the price received by the producer and the out of pocket expenditure of the consumer. Translating the concept to analytical language;

$$G = (P_1 - C_1)y_1 + (P_2 - C_2)y_2 + (P_0 - C_0)y_0. \quad (52)$$

Once again, taking first order derivative and evaluating in $\beta = 1$;

$$\left.\frac{\partial G}{\partial \beta}\right|_{\beta=1} = t\left(\frac{(1-\alpha)\big(43-l(35-6l)-\alpha(37l-23)\big)}{144}\right) < 0. \quad (53)$$

A small decrease in β, when the reference price is set by the cheapest generic, generates an increase in third payer share. This result is particularly important in what concerns public policy. At the same time, the rationale behind this effect is particularly easy to understand, given that, as was explained above, the increase of the influence of the expensive generic in r, not only increases all prices, but also decreases generic demand. The generic price increase has a particularly important effect here, once the third-payer's expenditure is only affected by the

reference price. The fact is that for a decreasing β the reference is deviating from the cheapest drug price, which by the way is also increasing its price. Concluding, we have three effects in the same direction, prices increase, demand shifts to expensive drugs and r is increasing. This way, the third payer ends spending more for each unit of the drug sold. To conclude this point, we will just add that this is one of most consensual topics of the literature on the theme, and it is no surprise that almost all reference systems define as reference the cheapest price, or the mean of the cheapest prices in each cluster.

Proposition 6: A marginal reduction in the relative weight of the cheapest generic on r, when $\beta = 1$, increases third payer expenditure.

4.4. Social welfare.

Social welfare is the sum of previous aggregates studied, total utility and total profits, minus third payer share. The idea now is to understand whether the society, as a whole, is better off with the definition of the cheapest generic within the cluster as reference. At this point, it is important to say that this variable does not measure the transfers between different agents within the society. In a certain way, and from this perspective, total welfare has no concerns on distribution justice or egalitarian wellbeing of the different agents. So, the previous analysis is not only necessary but also richer in what comes to political favoring one over another agent through political choice. Retaining all those issues, total welfare can be analytically described as the sum of previous variables;

$$W = Q + J - G. \tag{54}$$

Using the same methodology and taking the first order derivative and evaluating at point $\beta = 1$,

$$\left.\frac{\partial W}{\partial \beta}\right|_{\beta=1} = -t\left(\frac{(1-\alpha)(7-5l)(\mu(16-11l)+9l-6)}{(11+\mu)^3}\right) < 0. \tag{55}$$

Social welfare tends to increase when we deviate the reference from the cheapest generic in the market. The outcome achieved might be explained by the increased profits and the ambiguous effects on consumer's utility that such shift generates, since it increases third payer share as it was proved before. Gathering all information, we know now that a bigger influence of

the cheapest generic in reference scheme tends to decrease prices, increase cheap generic's market share, decrease total profits, third payer share, social welfare and has ambiguous effects on consumer's utility.

Proposition 7: A marginal reduction of the relative weight of the cheapest generic on r, when $\beta = 1$, increases social welfare.

Such result might be somehow surprising, since the model is telling us that a stricter reference system reduces total welfare. The fact is that the model described, with fixed total demand, implies that profits, third-payer's expenditures and consumer expenses eliminate each other. This means that we end up with a consumer surplus minus transportation costs. Those costs increase when consumers switch from the brand firm to both generic firms, given that the branded firm's consumers do not face them. Without favoring one agent against the others, what we have is a matter of income transfers.

Returning to the beginning of this chapter, we know that transportation costs are, from the consumer perspective, the perceived difference between the brand and any other generic drug. The importance of those costs drives us to a much more philosophical question - the meaning of such costs. Given that the bioequivalence of generic drugs has to be proved in order to allow any generic firm to enter the market, transportation costs might be seen as the confidence of consumers in the brand. If that is true, should policy makers concern about those costs? The history of policy decisions on the subject tells us that such costs are not the first concern of political makers. That can be alleged because the increase of generic drugs' market share is a target of many countries' pharmaceutical market policy. Here, we are focusing on another relevant issue, about what is the political target, or in other words, what is the policy maker's utility function.

In countries like Portugal, where pharmaceutical industry represents a small share of the gross domestic product, policy makers might be tempted to ignore profits, maximizing total utility and minimizing third payer share. The previous case is especially true for countries with a public health insurance system which is the case of many European countries. Economic intuition tells us that removing profits from political equation increases the incentives of regulatory policy to

trigger higher competition and lower prices. Using the model to try to answer those questions, we might create a new aggregate, say L, as a function of total Utility and third-payer's expenditures:

$$L = Q - G. \tag{56}$$

Using the same methodology:

$$\left.\frac{\partial L}{\partial \beta}\right|_{\beta=1} = t\,\frac{(1-\alpha)\left(22l^2-40l+82\right)}{1728} > 0. \tag{57}$$

As we might see in (55), the effect of a slight increase of the influence of the expensive generic and therefore a reduction in β decreases the aggregate L. Unlike total welfare, L is maximized for $\beta = 1$. Consequently, we now conclude that policy decision maker, or the society, in countries without their own pharmaceutical industry like Portugal, is better off setting reference pricing to the cheapest generic in the market. This outcome does not depend on the values assumed for α and *l*. This conclusion is somehow the one we were expecting, and what the economic literature analyzed indicates. Returning to literature review, we might now conclude that the schemes designed to induce generic entry, ether are more appealing to firms, come at a greater cost for consumers and third payer. However, questions explored around R&D, and innovative and generic drugs' market entry, which are not addressed in the model, should represent a major concern when defining regulatory policy.

Proposition 8: A marginal reduction in the relative weight of the cheapest generic on r, when $\beta = 1$, reduces the welfare of consumers and third payer as a whole.

5. Conclusion

Reference pricing has been one of the most popular policy measures in the western pharmaceutical markets. In this thesis, we look at the policy from a theoretical perspective. However, most of the conclusions derived from the developed model are in line with what empirical literature has been founding on the policy during the last few decades. We show how the variables that the policy maker has at his disposal influence the behavior of firms in the market. Concretely, we have shown how the rate of coinsurance and the influence of the different generics in the reference price manage to lower all prices.

The role of the cheapest generic in the market seems to be particularly important. The way the system manages to highlight its influence inside the reference is decisive to increase price competition between drugs. Our model is able to capture that importance through the slight advantage of the expensive generic drug, thus breaking the assumption of collusive behavior between generics. We conclude that a higher influence of the cheapest generic increases price elasticity of demand inducing higher generic market shares and lower prices.

Concerning the welfare analysis, the model conclusions meet our expectations since the influence of the cheapest generic seems to induce lower profits and lower third-payer's expenditure. That fact is particularly important in a conjuncture of severe restrictions on governments' expenditure which several policy adopting countries face. The influence of the cheapest generic on consumer's utility seems to be, however, ambiguous. That fact is directly connected to the consumers' perceived lower quality of generics. Sensitization campaigns in order to reduce that perceived difference might enhance generic consumption but also reduce brand prices.

We must assume, nevertheless, some limitations on the approach used. The model captures a market of an off-patent drug and the conclusions are limited to a generic reference pricing system. The therapeutic version of the scheme is likely to induce higher price competition even for the under patent drug in the cluster, as literature suggests. Yet, such version of the policy is out of the model scope. Another limitation to the model arises from the simplifications assumed. In fact, we assume no fixed or variable costs which limits the market sustainability analysis. Although it is not an over simplifying assumption, it would be interesting to understand how fixed or variable costs could influence firms market behaviors. Fixed costs could be

particularly important when it comes to generic entry. In our model we assured the presence of the three players in equilibrium, nonetheless, in a real market, the decision maker must define a sustainable market not only for firms within it, but also attractive to new generics that may increase competition.

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Annex

Empirical approaches:

Study	Time Period	Geographic Area	Effect on Prices	Effect on Market Shares
Moreno-Torres, Puig- Junoy, Raya (2010)	1995-2006	Spain	Price decreases (Only when pharmacists are obliged to dispense the generic cheaper version when the price of the prescribed drug is above RP)	-
Puig-Junoy, Moreno-Torres (2010)	1997-2009	Spain	Price decreases (only when reference is revised)	-
Dalen, Strom, Haabeth (2006) Note: Price cap regulation policy	1998-2004	Norway	Price decreases	Generic share increases Reduced market power
Danzon, Ketcham (2003)	1998	Germany, Netherlands, New Zealand	Lower prices under broader clusters.	Higher competition results in fewer entries of innovative drugs. Bigger countries suffer less from avoided entry of new drugs
Ghishlandi, Krulitchova, Garattini. (2005)	2001-2003	Italy	Price decreases	Generic share increases
Andersson et al. (2006)	1986	Sweden	Price decreases (Reduction in the slope of cost/DDD trend of increase for a short term)	-
Jaume Puig-Junoy (2007)	2001-2004	Spain	Price decreases (For off-patent drugs)	Overall impact on market sales was "Relatively modest".
Nina Pavcnik (2002)	1986-1996	Germany	Price decreases (Overall price reduction. More expressive for brands, with average price reduction of 21 to 26%)	-
rekke, Holmas, Straume(2011)	2001-2004	Norway	Price decreases (Overall reduction. More expressive in the case of brand (33%) than generics (22%)	Generic share increases

Theoretical Approaches:

Study	Comparison	Price	Market Coverage	Consumer surplus	Profit	Expenditure
Brekke, Holmas, Straume(2011)	No regulation versus Price cap.	$P^B \downarrow$, $P^G \downarrow$	$S^B \uparrow$, $S^G \downarrow$	-	-	-
	Price cap versus Endogenous RP.	$P^B \downarrow$, $P^G \downarrow$	$S^B \downarrow$, $S^G \uparrow$	-	-	-
	Increased influence of generic in endogenous RP function.	$P^B \downarrow$, $P^G \downarrow$	$S^B \downarrow$, $S^G \uparrow$	-	-	-
	Reduction of RP in exogenous system.	$P^B \downarrow$, $P^G \uparrow$	-	-	-	-
Marisa Miraldo (2009)	Introduction of a average or minimum RP policy. (2 firms without vertical differentiation)	Lower under Minimum RP	Higher for average RP	Higher for average RP	Higher for average RP	Higher in minimum RP
			(inverse before policy introduction)			
	Introduction of a average RP policy. (Market with 2 vertically and horizontally differentiated firms)	Increased	Unclear (depends on quality, co-payment and influence on RP function)	Unclear (depends on quality, co-payment and influence on RP function)	Unclear (depends on quality, co-payment and influence on RP function)	-
Jorge Mestre-Ferrándiz (2003)	Transition from reimbursement to Spanish reference pricing. (reference defined within an interval between Brand cost to $\bar{r}$.) **1**) $r =$ Brand cost **2**) $r \in (\text{Brand Cost}, \bar{r})$ **3)** $r = \bar{r}$	**1**) $P_{Brand} \downarrow, P_{Generic} =$ **2)** $P_{Brand} \downarrow, P_{Generic} \downarrow$ **3**)$P_{Brand} =$; $P_{Generic} \downarrow$	**1**) $q_B =; q_G =$ **2**) $q_B \uparrow;\ q_G =$ **3**) $q_B \uparrow; q_G \downarrow$	-	**1**) $\pi_B \downarrow; \pi_G =$ **2**) $\pi_B \uparrow$ or $\downarrow; \pi_G \downarrow$ **3**) $\pi_B \uparrow;\ \pi_G \downarrow$	**1**)$Exp_B \downarrow; Exp_G =$ **2**)$Exp_B \uparrow$ or $\downarrow;\ Exp_G \downarrow$ **3**)$Exp_B \uparrow; Exp_G \downarrow$
S. Ghislandi (2011)	Theoretical approach on	Prices are always lower				r is set to minimum

	generic competition in a RP system with r set endogenously.	on brand independence of r. Generics tend to collude around r				when there's BI and perfect elasticity. Leaving less expenditure to third payer and more out of pocket expenditure

European RPS:

Reference pricing systems in Europe		
With RP		Without RP
Belgium, Bulgaria, Croatia, Germany, Hungary, Italy, Latvia, Turkey	Czech Republic, Denmark, France, The Netherlands Poland, Portugal, Spain,	Austria, Norway, Sweden, UK.

Reference Schemes	
Scheme	Country
Average Price of all medicines	Croatia, Hungary
Average price of generics	France
Lowest price of all medicines	Bulgaria, Czech Republic, Finland, Hungary, Italy Latvia, Poland, Spain, Turkey
Lowest priced generic medicines	Bulgaria, Denmark, France , Lavia
Average of the five lowest priced generic medicines.	Portugal
Weighted average of all products in one group and calculated by regression analysis	Germany
Weighted average price of all medicines	The Netherlands

Clustering methods	
Method	Country
By active substance	Belgium, Bulgaria, Croatia,Czech republic, Denmark, Finland, France, Germany, Hungary, Italy, Latvia, Poland, Portugal Spain, Turkey.
By Pharmacological Class	Bulgaria, Croatia, Czech Republic, Germany, Hungary, The Netherlands.
By Therapeutic class	Croatia, Czech Republic, Germany, Hungary, Latvia, Poland.

Source: European Generic Medicines Association, cit by Dylst et al. 2012.